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LETTERS TO THE EDITOR

RE: "IS GULF WAR SYNDROME DUE TO STRESS? THE EVIDENCE REEXAMINED"

This letter is in response to the recent article by Robert Haley (1) in which he reviews the published literature on Persian Gulf War health issues and post-traumatic stress disorder (PTSD).

Dr. Haley is correct in his review when he states that virtually all studies done to date involving Persian Gulf War veterans have assessed PTSD using psychometric scales rather than clinical psychiatric interviews. He has also pointed out some of the potential biases associated with using psychometric scales to determine PTSD prevalence in studies of Persian Gulf War military personnel. However, we question the general applicability of the equation correcting for the sensitivity and specificity derived from clinical studies of Vietnam veterans with a high base rate of PTSD. For example, given a specificity of 90 percent, any study in which the observed prevalence of PTSD is ≤10 percent will yield 0 percent for the estimated "true" prevalence, because the numerator will always be negative. We disagree with the implication that the estimated "true" prevalence of PTSD is 0 percent in Persian Gulf War veterans. Validation studies of the psychometric scales are necessary for the study of PTSD in Persian Gulf War veterans specifically.

We have been studying a cohort of Persian Gulf War veterans since the spring of 1991 (2); subjects were first surveyed at Ft. Devens, Massachusetts, within 5 days of return from the Gulf (time 1, n = 2,949). As such, the Devens cohort represents a sample of US Army troops from New England-area units who were processed through Ft. Devens. Analysis of initial participating unit members indicated no discernable selection bias. The Devens cohort included US Army active, reserve, and National Guard veterans from over 80 different units. The most prevalent unit duties involved medical, military police, transportation, and engineering activities. Cohort members were deployed to many different locations in Saudi Arabia, Kuwait, and Iraq. The cohort was largely male (92 percent) and Caucasian (83 percent) and served in the National Guard (52 percent). In some respects, this differed from the troop duty status and ethnic breakdown of the total US Gulf force, which was 17 percent reserve and Guard troops and 68 percent Caucasian (3).

For the recently completed third phase of the study (time 3), we selected a stratified, random sample from the larger cohort and recruited subjects to complete a comprehensive study protocol that included several psychometric scales (e.g., Mississippi Scale for PTSD adapted for Desert Storm, M-PTSD-DS) and clinical diagnostic interviews for PTSD (Clinician Administered PTSD Scale, CAPS) and Axis I disorders (Structured Clinical Interview for DSMIII-R, SCID). A total of 141 persons completed the CAPS, as well as the M-PTSD-DS.

Based on time 3 data, the rates of current and lifetime PTSD as diagnosed by the CAPS are low in this particular Persian Gulf War cohort (5.0 percent current PTSD; 7.8 percent lifetime PTSD). The lifetime rate is comparable with the 7.8 percent rate obtained for a US community sample in the National Comorbidity Study reported by Kessler et al. (4). When measured by psychometric means using the M-PTSD-DS with a cutoff score of greater than 89, the rate of PTSD in this sample was 17.0 percent (sensitivity = 71.4 percent, specificity = 85.8 percent); when measured using a cutoff score of greater than 107, the rate of PTSD was 5.9 percent.

Even with the low prevalence of PTSD in this sample, we cannot conclude that the "true" rate of PTSD is 0 percent. Furthermore, the effect of PTSD on health outcomes should not be discounted. Research (5) and clinical experience suggest that it is essential to control for PTSD status in any analysis of health symptom reporting or neuropsychologic test performance, in studies of veterans' health status and illnesses. In the time 3 study, those persons with PTSD (n = 7) reported significantly higher rates of health symptoms (chi-square = 8.1 (1, n = 141, p = 0.004)). However, an appreciable number of persons reporting higher numbers of health symptoms (n = 60) do not meet criteria for PTSD. The findings suggest that increased health symptom reporting does not appear to be fully explained by PTSD status (or other psychiatric diagnoses), and other explanations must be explored.

References

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THE AUTHOR REPLIES

In their letter (1) regarding my article (2), Wolfe et al. graciously acknowledge the methodological fallacies that underlay the government policy that post-traumatic stress disorder (PTSD), or general life stress, was a major contributor to most illness in Gulf War veterans (3, 4). To my knowledge this is the first public acknowledgment of the policy error.

Throughout 1996 and 1997 the Presidential Advisory Committee on Gulf War Illness and others widely promoted the stress theory (3, 4), which arose from a misinterpretation of nondiagnostic psychometric screening scales, primarily the Mississippi PTSD scale (2). Simultaneously psychiatrists conducting definitive structured interviews for PTSD in Veterans Affairs medical centers were finding only rare cases of true PTSD but were not speaking out, presumably inhibited by the public policy.

Meanwhile our group identified veterans with signs of neurologic dysfunction strongly associated with risk factors for exposure to neurotoxic combinations of chemicals (5–7). Parallel experiments in animals confirmed that the implicated chemicals act synergistically to cause neurologic damage (8).

Recently, we studied several Gulf War veterans who developed subtle neurologic problems (e.g., temperature dysregulation, central sleep apnea, tremor) during or shortly after the war, have objective neurologic signs (e.g., pathologic nystagmus, saccadic slowing, asymmetric brainstem latencies, neuropsychologic indicators of organicity), and satisfy the criteria for PTSD. This suggests that a PTSD-like presentation might result from neurotoxic subcortical brain damage. Consequently, the diagnosis of PTSD should not be entertained in an ill Gulf War veteran until the appropriate neuropsychologic, neurophysiologic, and audiovestibular tests (6) have ruled out neurotoxic brain damage.

In their letter (1) Wolfe et al. report that 60 (43 percent) of 141 Gulf War veterans had symptoms of physical illness, not further characterized, whereas only seven (5 percent) had symptoms compatible with PTSD. If their population of Gulf War veterans is like those we studied, we would predict that a high proportion of those with physical symptoms, and perhaps all with apparent PTSD, would have subtle neurologic signs and abnormal results on the tests for neurotoxic brain damage and would give histories of wartime exposure to pesticides, high concentration insect repellants, putative low level chemical nerve agent, and/or advanced adverse effects from the pyridostigmine tablets. Unless this information is reported, structured PTSD interviews in Gulf War veterans cannot be interpreted. Their seven patients with PTSD may actually have neurotoxic brain damage, lacking the appropriate diagnostic workup.

Finally, Wolfe et al. question my approach for estimating the true (corrected) prevalence rate ($\hat{p}_c$) by adjusting the observed (uncorrected) prevalence rate ($\hat{p}_u$) for known sensitivity (U) and specificity (V) of the measurement method (2). The formula is correct (9); however, Wolfe et al. argue reductio ad absurdum that the possibility of obtaining $\hat{p}_c < 0$ invalidates the approach. First, however, under their hypothetic stipulation $V = 0.9$ and $0 < \hat{p}_u < 0.1$, they are incorrect in stating that $\hat{p}_c$ must be negative. $\hat{p}_c$ also depends on U (not stipulated in their example). Correcting for U raises $\hat{p}_c$ and could easily produce $\hat{p}_c \geq 0$ in their example. Second, if the correction is made with values of U and V from prior validation studies of the measurement method, these might vary enough from study to study to give a negative value for $\hat{p}_c$.

What is important here is that the psychometric PTSD scales were designed for screening, with U maximized (0.87–0.96) at the expense of very low V (0.57–0.83) (2). Valid ascertainment relies on follow-up structured interviews by physicians who can exclude the many false positives in patients with neurologic and other conditions that falsely elevate the screening scales. When surveys using these methods yield PTSD prevalence rates of the same magnitude as the false positive errors in measurement, the likelihood of erroneous interpretation (e.g., mistaking symptoms of neurotoxic brain damage for PTSD) is high.

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